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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,218	08/18/2000	Olga Yurieva	600-1-179N CON	6461

7590 11/20/2006

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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/642,218

Applicant(s)

YURIEVA ET AL.

Examiner

Richard G. Hutson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7,22,28,29,81,83-86,88,89 and 91-98 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 91-98 is/are allowed.
- 6) ☒ Claim(s) 7,22,28,29,81,83-86,88 and 89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/5/2006 has been entered.

Applicant's amendment of claim 7, cancellation of claims 8, 82, 87, 90 and the addition of new claims 91-98, in the paper of 9/5/2006, is acknowledged. Claims 7, 22, 28, 29, 81, 83-86, 88, 89 and 91-98 are still at issue and are present for examination. Applicants' arguments filed on 9/5/2006, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 22, 28, 29, 81, 83-86, 88 and 89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

Art Unit: 1652

the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 7, 22, 28, 29, 81, 83-86, 88 and 89. In response to this rejection applicants have amended claim 7, cancelled claims 8, 82, 87, 90, and added new claims 91-98 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the specification provides the polynucleotides of SEQ ID NOS: 1 and 3 as dnaX polynucleotides of *Thermus thermophilus* and that these two sequences are related in that SEQ ID NO: 3 is the coding sequence contained within SEQ ID NO: 1. Applicants submit these sequences as well as the identification of ATP-binding and Zn²⁺ finger consensus sites among the tau/gama subunits confirm that applicants were in possession of the claimed product. Applicants submit that given this data, persons of skill in the art would have expected other members of the *Thermus* genus to possess a similar structure and function to that demonstrated for dnaX and the tau/gamma subunits of SEQ ID NOS: 1, 3, 2, 4 and 5.

Applicants submit that the evidence previously presented and presented as Exhibits A-C demonstrate that the species of SEQ ID NOS: 1 and 3 adequately represent the claimed subject matter. Applicants submit McHenry et al. (J. Mol. Biol. 272:178-189, 1997) identifies the 63 and 50 kDA protein products of the *T. thermophilus* dnaX gene as the g and t subunits of *T. thermophilus* and that those sequences identified by McHenry et al. share 98% and 97% homology, respectively, with those of the present application. Additionally, applicants present Genbank accessions which

Art Unit: 1652

identify the coding sequence and encoded tau products for *T. thermophilus* strains HB8 and HB27, respectively. Applicants thus submit that the alignment of these sequences supports that the species of dnaX from thermophilic organisms belonging to the biological classification *Thermus* share similar structure and therefore function.

Applicants further submit that the language recited in claim 7 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under written description requirement.

Applicants thus submit that based upon the above, the previous conclusion by the PTO is contrary to evidence submitted herewith by applicants and that one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention.

Applicant's amendment and arguments are acknowledged and have been carefully considered, however, have been found to be non-persuasive in overcoming the instant rejection based upon a lack of written description. While applicants argue that the presently claimed genus shares similar structure and thus function based upon this "similar structure", this conclusion remains in question. Applicant's claims are drawn to those nucleic acids encoding tau and gamma subunits of a DNA polymerase III-type enzyme and these "functions" in combination with the structural limitations of the claims are insufficient to meet the requirement for the written description of the claimed genus. It remains that applicants have not adequately described a structure-to-function relationship given that the "function" of the claimed nucleic acids remains in question.

Art Unit: 1652

What is the function associated with the tau and gamma subunits of a DNA polymerase III-type enzyme and how does it relate to referred to structure?

Applicants comparison to the decision in the Univ. of California v. Eli Lilly, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) is acknowledged, however, as stated above, the recited function in the instantly claimed genus remains not as clear as that in the referred to case law, and thus any comparison to a decision based upon this is considered flawed.

The Guidelines for Examination of Patent Applications Under 35 USC 112 1st Paragraph, 'Written Description Requirement' make explicitly clear that the description of a representative number of species does not require the description to be of such nature that it would provide support for each species that the genus embraces, is acknowledged, however, given the necessary function of the encoded proteins, it remains that a sufficient structure-to-function relationship has not been established for the currently claimed genus.

Applicant is referred to the guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 7, 22, 28, 29, 81, 83-86, 88 and 89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a τ or γ subunit of a DNA polymerase III-type enzyme, wherein said τ or γ subunit has an amino acid residue sequence represented by the formula

shown in SEQ ID NO: 2 or SEQ ID NO: 4, does not reasonably provide enablement for any polynucleotide encoding a τ or γ subunit of a DNA polymerase III-type enzyme of a thermophilic bacterium, wherein said polynucleotide is a mere 90% identical to the nucleotide sequence of SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 7, 22, 28, 29, 81, 83-86, 88 and 89. In response to this rejection applicants have amended claim 7, cancelled claims 8, 82, 87, 90, and added new claims 91-98 and traverse the rejection as it applies to the newly amended claims.

Applicants continue to traverse the rejection on the basis that all that is needed is objective enablement of what is claimed and the present application provides the nucleotide sequence of a *Thermus thermophilus* dnaX (e.g., SEQ ID NOs: 1 and 3) and describes how one of ordinary skill can isolate other homologs of the disclosed sequence, and express the tau and gamma subunits and test the subunits for activity.

Applicants continue to argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification teaches the complete nucleotide sequences of a *Thermus thermophilus* dnaX, protocols for using the DNA of SEQ ID NO:1 as a probe, and protocols for testing for the encoded proteins activity as well as methods of identifying and producing variants of *T. thermophilus* Pol III γ and τ subunits are known by those skilled in the art. Applicants support their assertions regarding

Art Unit: 1652

methods of identifying and producing variants by presenting the publication by McHenry et al.

Applicants complete argument has been considered, however, not found persuasive for the reasons previously stated and repeated below.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a DNA polymerase type-III subunit) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the larger number of variants have the desired properties. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting τ or γ subunit activity; (B) the general tolerance of τ or γ subunits to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a DNA polymerase III enzyme τ or γ subunit with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack

Art Unit: 1652

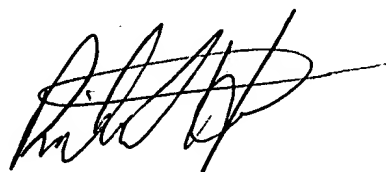
of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the delta subunit activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those DNA molecules of the claimed genus which encode a polypeptide with DNA polymerase III enzyme τ or γ subunit activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the claimed DNA molecules from a *Thermus* bacterium, encoding a DNA polymerase III-type enzyme τ or γ subunit. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'R. G. Hutson', with a long horizontal stroke extending to the right.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rg
11/2/2006